CLAIMS

1. A method of evaluating assay data that is arranged in a three dimensional array, the assay being subject to systematic and positional effects, the method comprising:

compensating the raw assay data for the systematic and positional effects;

scoring the compensated data; and

formatting the scored data according to a determined format.

2. The method of claim 1 wherein an assay is performed to generate a compendium of raw assay data that is then compensated for systematic and positional effects.

3. The method of claim 1 wherein the raw assay data is generated from a high throughput screening assay to identify a biologically active agent in a collection of test agents, wherein a biologically active agent is identified by identifying a test agent that generates a data point which statistically deviates from other data points in the formatted scored data.

4. The method of claim 1 wherein the raw assay data is generated from a high throughput screening assay to identify a pharmacologically active agent in a collection of test agents,

wherein

the high throughput screening assay is selected from the group consisting of enzyme activation, enzyme inhibition, ligand-receptor binding, ligand-receptor binding inhibition, cell cycle inhibition, cell cycle

activation, cell growth, cell division, cell activation, cell inhibition, activation of production of and/or release of cellular factors, inhibition of production of and/or release of cellular factors, ion pump, transport or channel activity, ion pump, transport or channel inhibition, activation of DNA synthesis, inhibition of DNA synthesis, activation of RNA synthesis, inhibition of RNA synthesis, activation of protein synthesis, inhibition of protein synthesis, metabolic activity, metabolic inhibition, activation of apoptosis, and inhibition of apoptosis,

the collection of test agents is selected from the group consisting of: chemically synthesized molecules, natural products, cell extracts, nucleic acid molecules, cell culture media, proteins, isolated genetic material, fungal extracts and microbial fermentation broths; and recombinant products, viral particles, phage particles, proteins and peptide libraries; and

the pharmacologically active agent is identified by identifying a test agent that generates a data point which statistically deviates from other data points in the formatted scored data.

5. The method of claim 1 comprising performing an assay such that a compendium of raw assay data is developed in a computer-readable form for purposes of allowing a computer-based algorithm to operate on such data.

6. The method of claim 1 comprising compensating the raw assay data for systematic and/or positional effects by way of a computer-based algorithm.

7. The method of claim 1 wherein the raw data has row-based aspects, column-based aspects, and non-additive interaction-based aspects, the method comprising compensating the raw assay data for row-based positional effects.

8. The method of claim 1 wherein the raw data has row-based aspects, column-based aspects, and non-additive interaction-based aspects, the method comprising compensating the raw assay data for column-based positional effects.

9. The method of claim 1 wherein the raw data has row-based aspects, column-based aspects, and non-additive interaction-based aspects, the method comprising compensating the raw assay data for longitudinal-based positional effects.

10. A method of positionally correcting raw assay data from an assay comprising a plurality of longitudinally oriented plates p, each plate p having a plurality of wells organized into rows i and columns j, each well (i, j, p) having a raw value x_{ijp} associated therewith, the raw values x_{ijp} comprising the raw assay data, the method comprising deconstructing each raw value x_{ijp} of an associated well (i, j, p) into:

a plate effect value representing extraneous effects attributable to the plate p of the well (i, j, p);

a row effect value representing extraneous effects attributable to the row i on the plate p of the well (i, j, p);

a column effect value representing extraneous effects attributable to the column j on the plate p of the well (i, j, p);

a non-additive, interaction effect value representing extraneous positional effects attributable to consistent positional effects beyond the plate, row, and column effects previously determined for the (i, j, p) well on plate p; and

a residual data value that is left over once all the above extraneous effects are taken into account,

the method further comprising employing the residual data value associated with

each well (i, j, p) to represent the well (i, j, p) as compared with all other wells (i, j, p) on the plate p.

11. The method of claim 10 wherein the raw assay data is generated from a high throughput screening assay to identify a biologically active agent in a collection of test agents, wherein the assay is subject to positional and systemic effects, the raw assay data is arranged in a three dimensional array, a biologically active agent is identified by identifying a test agent that generates a data point which statistically deviates from other data points in the formatted scored data.

12. The method of claim 10 comprising employing the residual data value associated with each well (i, j, p) to represent the well (i, j, p) as compared with all other wells (i, j, p) on all of the plates p.

13. The method of claim 10 comprising deconstructing each raw value x_{ijp} of an associated well (i, j, p) into a plate effect value representing the overall median of all the raw values of the wells on plate p.

14. The method of claim 13 comprising deconstructing each raw value x_{ijp} of an associated well (i, j, p) into a row effect value representing the median of all the raw values of the wells for row i on plate p after taking into consideration the plate effect value.

15. The method of claim 13 comprising deconstructing each raw value x_{ijp} of an associated well (i, j, p) into a column effect value representing the median of all the raw values of the wells for column j on plate p after taking into consideration the plate effect value.

16. The method of claim 10 comprising deconstructing each raw value x_{ijp} of an associated well (i, j, p) into a non-additive, interaction effect value representing an additional possible systematic measurement effect beyond the plate, row, and column effect values previously determined for the (i, j, p) well on plate p.

17. A method of positionally correcting raw assay data from an assay comprising a plurality of longitudinally oriented plates p, each plate p having a plurality of wells organized into rows i and columns j, each well (i, j, p) having a raw value x_{ijp} associated therewith, the raw values x_{ijp} comprising the raw assay data, the method comprising:

resistantly fitting the raw value x_{ijp} for each well (i, j) for each plate p to a row-column additive model:

$$y_{ijp} = \mu_p + R'_{ip} + C'_{jp} + e_{ijp} \ .$$

where:

y_{ijp} = the raw value for the well at row i and column j on plate p;

μ_p = an overall "average" for plate p;

R'_{ip} = a possible systematic measurement row offset for row i on plate p;

C'_{jp} = a possible systematic measurement column offset for column j on plate p; and

e_{ijp} = residual data without taking into account any non-additive interaction offset;

longitudinally (plate-wise) non-linearly smoothing each R'_{ip} and each C'_{jp};

substituting each un-smoothed R'_{ip} and C'_{jp} value with a corresponding smoothed R_{ip} and C_{jp} value and adjusting each residual value e_{ijp}

to an adjusted e'_{ijp}:

$$y_{ijp} = \mu_p + R_{ip} + C_{ip} + e'_{ijp} \ ;$$

longitudinally (plate-wise) non-linearly smoothing each e'_{ijp} to result in:

$$y_{ijp} = \mu_p + R_{ip} + C_{jp} + \text{smooth}_p(e'_{ijp}) + r_{ijp}$$

where each e'_{ijp} is deconstructed into $\text{smooth}_p(e'_{ijp})$, a possible systematic non-additive interaction offset for the (i, j) well on plate p, and r_{ijp}, residual data left over after taking into account any interaction offset;

wherein each r_{ijp} represents a true relative value of the corresponding well (i, j, p) as compared to all other wells (i, j, p) on the plate p.

18. The method of claim 17 wherein the raw assay data is generated from a high throughput screening assay to identify a biologically active agent in a collection of test agents, wherein the assay is subject to positional and systemic effects, the raw assay data is arranged in a three dimensional array, a biologically active agent is identified by identifying a test agent that generates a data point which statistically deviates from other data points in the formatted scored data.

19. The method of claim 17 comprising resistantly fitting the raw value x_{ijp} for each plate p to a row-column additive model according to a two way resistant median polish procedure.

20. The method of claim 17 comprising longitudinally (plate-wise) non-linearly smoothing each R'_{ip} and each C'_{jp} according to one of a running median smoother and a lowess procedure.

21. The method of claim 17 comprising longitudinally (plate-wise) non-linearly smoothing each e'_{ijp} according to one of a running median smoother and a lowess procedure.

22. The method of claim 17 further comprising normalizing each r_{ijp} to result in a true relative value of the corresponding well (i, j, p) that can be compared to all other wells (i, j, p) on all plates p.

23. The method of claim 22 comprising normalizing each r_{ijp} by a standard deviation value derived from all the r_{ijp}'s on the plate p to result in a score for the well (i, j, p) that can be compared across plates p:

$$score_{ijp} = r_{ijp} / (\text{standard deviation value})_p .$$

24. The method of claim 23 comprising normalizing each r_{ijp} by a median absolute deviation from median value.

25. A computer having computer modules executing thereon for positionally correcting raw assay data from an assay comprising a plurality of longitudinally oriented plates p, each plate p having a plurality of wells organized into rows i and columns j, each well (i, j, p) having a raw value x_{ijp} associated therewith, the raw values x_{ijp} comprising the raw assay data, the modules comprising a first module deconstructing each raw value x_{ijp} of an associated well (i, j, p) into:

a plate effect value representing extraneous effects attributable to the plate p of the well (i, j, p);

a row effect value representing extraneous effects attributable to the row i on the plate p of the well (i, j, p);

a column effect value representing extraneous effects attributable to the column j on the plate p of the well (i, j, p);

a non-additive, interaction effect representing extraneous positional effects attributable to consistent positional effects beyond the plate, row, and column effects determined for the (i, j, p) well on plate p; and

a residual data value that is left over once all the above extraneous effects are taken into account, the computer further comprising a second module employing the residual data value associated with each well (i, j, p) to represent the well (i, j, p) as compared with all other wells (i, j, p) on the plate p.

26. The computer of claim 25 wherein the raw assay data is generated from a high throughput screening assay to identify a biologically active agent in a collection of test agents, wherein a biologically active agent is identified by identifying a test agent that generates residual data value which statistically deviates from other residual data values generated.

27. The computer of claim 25 wherein the second module employs the residual data value associated with each well (i, j, p) to represent the well (i, j, p) as compared with all other wells (i, j, p) on all of the plates p.

28. The computer of claim 25 wherein the first module deconstructs each raw value x_{ijp} of an associated well (i, j, p) into a plate effect value representing the overall median of all the raw values of the wells on plate p.

29. The computer of claim 28 wherein the first module deconstructs each raw value x_{ijp} of an associated well (i, j, p) into a row effect value representing the median of all the raw values of the wells for row i on plate p after taking into consideration the plate effect value.

30. The computer of claim 28 wherein the first module deconstructs each raw value x_{ijp} of an associated well (i, j, p) into a column effect value representing the median of all the raw values of the wells for column j on plate p after taking into consideration the plate effect value.

31. The computer of claim 25 wherein the first module deconstructs each raw value x_{ijp} of an associated well (i, j, p) into a non-additive interactive effect value representing possible systematic measurement effect for the (i, j) well on plate p beyond that attributable to the plate, row and column effect values.

32. The computer of claim 25 further comprising an inputting module inputting the raw values x_{ijp} into a data structure in a memory of the computer, whereby the first module accesses the raw values x_{ijp} from the data structure.

33. A computer having computer modules executing thereon for positionally correcting raw assay data from an assay comprising a plurality of longitudinally oriented plates p, each plate p having a plurality of wells organized into rows i and columns j, each well (i, j, p) having a raw value x_{ijp} associated therewith, the raw values x_{ijp} comprising the raw assay data, the modules comprising:

a first module resistantly fitting the raw value x_{ijp} for each well (i, j) for each plate p to a row-column additive model:

$$y_{ijp} = \mu_p + R'_{ip} + C'_{jp} + e_{ijp} \ .$$

where:

y_{ijp} = the raw value for the well at row i and column j on plate p;

μ_p = an overall "average" for plate p;

R'_{ip} = a possible systematic measurement row offset for row i on plate p;

C'_{jp} = a possible systematic measurement column offset for column j on plate p; and

e_{ijp} = residual data without taking into account any non-additive interaction offset;

a second module longitudinally (plate-wise) non-linearly smoothing each R'_{ip} and each C'_{jp};

a third module substituting each un-smoothed R'_{ip} and C'_{jp} value with a corresponding smoothed R_{ip} and C_{jp} value and adjusting each residual value e_{ijp} to an adjusted e'_{ijp}:

$$y_{ijp} = \mu_p + R_{ip} + C_{ip} + e'_{ijp} \text{ ; and}$$

a fourth module longitudinally (plate-wise) non-linearly smoothing each e'_{ijp} to result in:

$$y_{ijp} = \mu_p + R_{ip} + C_{jp} + \text{smooth}_p(e'_{ijp}) + r_{ijp}$$

where each e'_{ijp} is deconstructed into $\text{smooth}_p(e'_{ijp})$, a possible systematic non-additive interaction offset for the (i, j) well on plate p and r_{ijp} residual data value left over after taking into account any non-additive interaction offset;

wherein each r_{ijp} represents a true relative value of the corresponding well (i, j, p) as compared to all other wells (i, j, p) on the plate p.

34. The computer of claim 33 wherein the raw assay data is generated from a high throughput screening assay to identify a biologically active agent in a collection of test agents, wherein a biologically active agent is identified by identifying a test agent that generates an r_{ijp} which statistically deviates from r_{ijp}

generated.

35. The computer of claim 33 wherein the first module resistantly fits the raw value x_{ijp} for each plate p to a row-column additive model according to a two way resistant median polish procedure.

36. The computer of claim 33 wherein the second module longitudinally (plate-wise) non-linearly smoothes each R'_{ip} and each C'_{jp} according to one of a running median smoother and a lowess procedure.

37. The computer of claim 33 wherein the fourth module longitudinally (plate-wise) non-linearly smoothing each e'_{ijp} according to one of a running median smoother and a lowess procedure.

38. The computer of claim 33 further comprising a fifth module normalizing each r_{ijp} to result in a true relative value of the corresponding well (i, j, p) that can be compared to all other wells (i, j, p) on all plates p.

39. The computer of claim 38 wherein the fifth module normalizes each r_{ijp} by a standard deviation value derived from all the r_{ijp}'s on the plate p to result in a score for the well (i, j, p) that can be compared across plates p:

$$score_{ijp} = r_{ijp} / (\text{standard deviation value})_p .$$

40. The computer of claim 39 wherein the fifth module normalizes each r_{ijp} by a median absolute deviation from median value.

41. The computer of claim 33 further comprising an inputting module inputting the raw values x_{ijp} into a data structure in a memory of the

computer, whereby the first module accesses the raw values x_{ijp} from the data structure.

42. A computer-readable medium having computer-executable modules thereon for positionally correcting raw assay data from an assay comprising a plurality of longitudinally oriented plates p, each plate p having a plurality of wells organized into rows i and columns j, each well (i, j, p) having a raw value x_{ijp} associated therewith, the raw values x_{ijp} comprising the raw assay data, the modules comprising a first module for deconstructing each raw value x_{ijp} of an associated well (i, j, p) into:

a plate effect value representing extraneous effects attributable to the plate p of the well (i, j, p);

a row effect value representing extraneous effects attributable to the row i on the plate p of the well (i, j, p);

a column effect value representing extraneous effects attributable to the column j on the plate p of the well (i, j, p);

a non-additive, interaction effect representing extraneous positional effects attributable to systematic positional effects beyond the plate, row, and column effects previously determined for the (i, j, p) well on plate p; and

a residual data value that is left over once all the above extraneous effects are taken into account,

the computer further comprising a second module for employing the residual data value associated with each well (i, j, p) to represent the well (i, j, p) as compared with all other wells (i, j, p) on the plate p.

43. The computer-readable medium of claim 42 wherein the raw assay data is generated from a high throughput screening assay to identify a biologically active agent in a collection of test agents, wherein a biologically active agent is identified by identifying a test agent that generates a residual data value which statistically deviates from the other residual data value generated by the

assay.

44. The computer-readable medium of claim 42 wherein the second module employs the residual data value associated with each well (i, j, p) to represent the well (i, j, p) as compared with all other wells (i, j, p) on all of the plates p.

45. The computer-readable medium of claim 42 wherein the first module deconstructs each raw value x_{ijp} of an associated well (i, j, p) into a plate effect value representing the overall median of all the raw values of the wells on plate p.

46. The computer-readable medium of claim 45 wherein the first module deconstructs each raw value x_{ijp} of an associated well (i, j, p) into a row effect value representing the median of all the raw values of the wells for row i on plate p after taking into consideration the plate effect value.

47. The computer-readable medium of claim 45 wherein the first module deconstructs each raw value x_{ijp} of an associated well (i, j, p) into a column effect value representing the median of all the raw values of the wells for column j on plate p after taking into consideration the plate effect value.

48. The computer-readable medium of claim 42 wherein the first module deconstructs each raw value x_{ijp} of an associated well (i, j, p) into a non-additive interactive effect value representing a possible systematic measurement effect for the (i, j) well on plate p with respect to (i, j) wells on nearby plates p.

49. The computer-readable medium of claim 42 further comprising an inputting module inputting the raw values x_{ijp} into a data structure in

a memory of a computer, whereby the first module accesses the raw values x_{ijp} from the data structure.

50. A computer-readable medium having computer-executable modules thereon for positionally correcting raw assay data from an assay comprising a plurality of longitudinally oriented plates p, each plate p having a plurality of wells organized into rows i and columns j, each well (i, j, p) having a raw value x_{ijp} associated therewith, the raw values x_{ijp} comprising the raw assay data, the modules comprising:

a first module for resistantly fitting the raw value x_{ijp} for each well (i, j) for each plate p to a row-column additive model:

$$y_{ijp} = \mu_p + R'_{ip} + C'_{jp} + e_{ijp} \ .$$

where:

y_{ijp} = the raw value for the well at row i and column j on plate p;

μ_p = an overall "average" for plate p;

R'_{ip} = a possible systematic measurement row offset for row i on plate p;

C'_{jp} = a possible systematic measurement column offset for column j on plate p; and

e_{ijp} = residual data without taking into account any non-additive interaction offset;

a second module for longitudinally (plate-wise) non-linearly smoothing each R'_{ip} and each C'_{jp};

a third module for substituting each un-smoothed R'_{ip} and C'_{jp} value with a corresponding smoothed R_{ip} and C_{jp} value and adjusting each residual value e_{ijp} to an adjusted e'_{ijp}:

$$y_{ijp} = \mu_p + R_{ip} + C_{ip} + e'_{ijp} \text{ ; and}$$

a fourth module for longitudinally (plate-wise) non-linearly smoothing each e'_{ijp} to result in:

$$y_{ijp} = \mu_p + R_{ip} + C_{jp} + \text{smooth}_p(e'_{ijp}) + r_{ijp}$$

where each e'_{ijp} is deconstructed into $\text{smooth}_p(e'_{ijp})$, a possible systematic non-additive interaction measurement offset for the (i, j) well on plate p, and r_{ijp}, residual data left over after taking into account any interaction offset;

wherein each r_{ijp} represents a true relative value of the corresponding well (i, j, p) as compared to all other wells (i, j, p) on the plate p.

51. The computer-readable medium of claim 50 wherein the raw assay data is generated from a high throughput screening assay to identify a biologically active agent in a collection of test agents, wherein a biologically active agent is identified by identifying a test agent that generates an r_{ijp} which statistically deviates from the r_{ijp} generated by the other agents in the assay.

52. The computer-readable medium of claim 50 wherein the first module resistantly fits the raw value x_{ijp} for each plate p to a row-column additive model according to a two way resistant median polish procedure.

53. The computer-readable medium of claim 50 wherein the second module longitudinally (plate-wise) non-linearly smoothes each R'_{ip} and each C'_{jp} according to one of a running median smoother and a lowess procedure.

54. The computer-readable medium of claim 50 wherein the fourth module longitudinally (plate-wise) non-linearly smoothing each e'_{ijp} according to one of a running median smoother and a lowess procedure.

55. The computer-readable medium of claim 50 further comprising a fifth module for normalizing each r_{ijp} to result in a true relative value of the corresponding well (i, j, p) that can be compared to all other wells (i, j, p) on all plates p.

56. The computer-readable medium of claim 55 wherein the fifth module normalizes each r_{ijp} by a standard deviation value derived from all the r_{ijp}'s on the plate p to result in a score for the well (i, j, p) that can be compared across plates p:

$$score_{ijp} = r_{ijp} / (\text{standard deviation value})_p .$$

57. The computer-readable medium of claim 56 wherein the fifth module normalizes each r_{ijp} by a median absolute deviation from median value.

58. The computer-readable medium of claim 50 further comprising an inputting module for inputting the raw values x_{ijp} into a data structure in a memory of a computer, whereby the first module accesses the raw values x_{ijp} from the data structure.